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THE
HYPODERMIC USE OF MERCURIALS
IN THE
TREATMENT OF SYPHILIS.

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THE introduction of hypodermic medication by Alex. Wood, in 1857, was soon followed by various investigators and experimenters with mercurials, applied in a similar manner. Among them was Hebra, in 1860, who noted from injections of corrosive sublimate, dissolved in water, a rapid deflorescence of specific eruptions in the neighborhood (?) of the puncture. Scarenzio, in 1864, injected calomel, suspended in mucilaginous fluids, and reported eight cases with highly satisfactory results. He was closely followed by Ambrosi, Ricord, and Montefork with like results, and their observations were confirmed by Berkley Hill in England and Bergh in Denmark.

Thus far the method was largely experimental, and not until Lewin, in Berlin, published the results of many cases successfully treated with injections of corrosive sublimate at the Charité Hospital in Berlin did the



hypodermic medication with mercuric sublimate find more general recognition and application. He proved, while starting with $\frac{1}{12}$ to $\frac{1}{8}$ grain, that injections of even $\frac{1}{2}$ to 1 grain might be made without fatal or serious consequence. Citing the cases of one hundred and forty-four males and three hundred and fifty-six females, or a total of five hundred patients, he deduced that the total amount of the mercuric salt necessary to cause a complete disappearance of all symptoms to have been for males .17 gramme, or about three grains, while for females only .135 gramme, or a little over two grains, sufficed. Salivation was reported to have occurred in seventeen and a half per cent., and relapses were noted in only thirty-seven and a half per cent., against eighty-six per cent. of relapses by the other methods practised before that period at the Charité. Lewin concludes that the symptoms disappear in a ratio of rapidity with the amount of sublimate injected.

Lewin's observations were soon confirmed by those made at the clinics of Sigmund and Zeissl in Vienna, where the hypodermic injections of calomel were also further studied. Zeissl observed that .02 gramme, or $\frac{1}{3}$ grain, of the mild mercurial chloride, suspended in glycerin and water, and injected every day, brought about disappearance of the milder cutaneous syphilides within two to three days, and that, as a rule, a total of .3 gramme (five grains) to .5 gramme (seven and a half grains) of calomel administered in this way sufficed to abate all visible symptoms. He deduced that the greatest objec-

tion to this mode of treatment is the pain it gives rise to, both at the time of the injection as well as for some time afterwards, together with the formation of nodules in the connective tissue, which are both painful and last for some time, making exertions and physical labor almost impossible ; this is more marked after calomel injections than after those with corrosive sublimate, though the former bring about more rapid disappearance of symptoms ; ptyalism is not more frequent by this method than by the inunction treatment, and is less so with the sublimate than with calomel, and for that and other reasons he gives the corrosive sublimate the preference. A curious fact is cited that, while the gingivitis from inunctions affects the gums around the upper incisors principally, that of the hypodermic treatment with mercurials seems to affect those of the lower maxillary only. The pain and indurations produced by the subcutaneous injections of both sublimate and calomel soon led to the employment of compounds of mercury, which were to obviate these disadvantages. Arguing from the inference that the corrosive sublimate would be converted by the albuminous fluids of the cellular tissue into an insoluble mercuric albuminate, which, in turn, would be gradually dissolved by the excess of albumen and alkaline chlorides, both Staub and Bamberger were led to originate and employ a soluble albuminate of mercury, which *à priori* would appear a desideratum. However, the results with it were^s both unsatisfactory in regard to their curative results as well as to the painless administration of the mercurial, and

were soon abandoned to give way to Bamberger's mercuric peptonate, which, while claimed to give less pain, appears not to give satisfactory results, as will be seen hereafter.

Other mercurials, such as the mercuric iodide, dissolved in potassium iodide, the mercuric cyanide, the mercuric formamidate, enjoyed an ephemeral popularity and reputation, but fell in disrepute when clinically tested and their results compared with those of calomel or corrosive sublimate. A combination of analgesics (morphine, cocaine) were admixed to their solutions, but rapidly crystallized therefrom as mercuric-alkaloidal-amides.

This brings us to the present decade, and with it a renewed interest in these methods. Though the work of Lewin had been early translated and published in this country, the new mode of treatment has never enjoyed a reputation in American practice, and while syphilographers gave it room in their treatises, they held aloof from committing themselves as to its results or recommending it to their followers. As much may be said of English practitioners, and the teutophobe French would hardly laud the good that came from Berlin. Thus, while Berlin and Vienna injected with excellent results, and piled up their statistics to many thousand cases, they stood alone in its praise. Liebreich in 1883 introduced the mercuric formamidate for hypodermic use, for which it is claimed that it rapidly exhibited its curative effect if injected in doses of from 10 to 20 minims of a one per cent. solution,

that it does not often produce ptyalism, and gives rise to little or no pain (*Med. Times and Gazette*, January 6, 1883).

Delpach (*Thèse de Paris*, July, 1883) recommends the ammoniated mercurial peptonate for hypodermic use, which, he says, does not give rise to pain nor produce abscesses, etc. Its action, he claims, is most rapid, and readily reduces the severest lesions, without danger of salivation, in doses of 10 milligrammes ($\frac{1}{6}$ grain), while it obviates the gastro-intestinal irritation following the internal use of mercurials. Watrazenski, of Warsaw, in 1886 (*Centralblatt f. d. Med. Wissenschaften*), revived the injections of insoluble mercurials, and, after experimenting with calomel for some time, became dissatisfied with them, and proposed the mercuric, and also the mercurous oxides, suspended in water and mucilage, in doses of .06 to .1 gramme (1 to $1\frac{1}{2}$ grains) repeated every six to eight days. Three to five injections like these suffice to bring the symptoms to abeyance. The oxides, according to him, cause little or no pain (?), nor do they produce abscesses, and he thinks the mercurous oxides the milder of the two in their action. Dr. Edward Lang (*Wiener Medizinische Wochenschrift*, Nos. 34 and 35) further introduces a new mercurial for hypodermic medication, which he terms "oleum cinereum," or gray oil. He prepares it in a manner similar to that in which mercurial ointment is made, but uses oils and fats instead of the more solid fats, and of a strength that each cubic centimetre of the twenty per cent. oil contains .23 gramme (four grains) of mercury. Of this he

injects about $\frac{1}{10}$ cubic centimetre, and even $\frac{2}{10}$ to $\frac{3}{10}$ cubic centimetre once or twice a week, but often one injection every two weeks suffices, as larger quantities or more frequent repetition may cause pyalism. He recommends these injections especially in adenitis, when the injections should be made near the glands, as well as in the periosteal gummata of the forehead, when the injections are to be made near their borders.

Kopp and Choten (*Vierteljahreschrift für Dermat. und Syph.*, 1886, 4, ii.) report two hundred and sixty-three cases which they had treated with satisfactory results at Neisser's clinic in Breslau, according to Scarenzio's method, with hypodermic injections of calomel. They made a total number of fifteen hundred and twenty-three injections, and observed among these seventy-two abscesses. They recommended the following formula as the best in their experience :

R Hydrarg. chlorid. mit. (vapore parat.), ℥iv;
Sodii chloridi, ℥i;
Aquæ destillatæ, f℥ii. M.

Of this, they claimed four injections, given in two sittings, two weeks apart, were sufficient to abate all symptoms ; also that the sodium chloride present caused the formation of some mercuric chloride, thus preventing the formation of lower organisms. With proper cleanliness and the injections made in the gluteal region and the connective tissue thereof, they think its effect as sure, with a minimum of injections needed and cheapness of material, while occasional abscesses,

uncertainty of dosage, and relapses are some of the disadvantages.

Dr. Balzer, at the Lourcine Hospital in Paris, experimented largely with the hypodermic injections of calomel, according to the method of Scarenzio and Smirnoff, by making a small number of injections deep into the muscular tissues. He introduced the employment of vaseline oil as excipient, instead of the usual water and glycerin. The formula employed by him is as follows :

R Hydrarg. chlorid. mit., .5 gramme (gr. viiss);
Olei vaselinæ, 10 grammes (ʒiiss). M.

Dr. Besnier, at his clinics at the Hôpital St. Louis in Paris, approved of these methods as desirable modifications of the internal treatment by mercurials, which too often caused dyspepsia, stomatitis, etc., and often led to grave disappointments. He thought the calomel injections as of greater value than those with sublimate, on account of giving less pain (?) and requiring a smaller number of injections. He thinks the method of Scarenzio far superior, as the calomel is gradually changed into mercuric chloride, and .40 to .50 gramme (6 to $7\frac{1}{2}$ grains) suffice for a cure (?). He notes the occasional occurrences of phlegmons and abscesses and the pain connected with it, but its revival is no doubt due to its manifest good effect. Balzer's employment of vaseline oil as a menstruum he considers a great improvement, but also urges strict sterilization of the calomel and rigid antiseptic precautions. He does not confine his patients to

bed for three days, as recommended by others. Twenty-four to forty-eight hours after the injection the inflammatory reaction takes place, and a slight œdematous swelling about the injected calomel, a small nodule, painful to the touch, remains for eight days subsequently. With all due precautions abscesses were not avoided in some of the cases.

The question of hypodermic medication of syphilis with mercurials was the great point of interest at this time (1887) in the hospitals and medical societies of Paris (Paris letters of the *Journal of Cutaneous and Genito-Urinary Diseases*). Du Castel, at the Hôpital du Midi, used .10 gramme ($1\frac{1}{2}$ grains) in vaseline oil for injections carried deep into the muscles of the buttocks at intervals of eight days. Phlegmons and painful nodules appeared at their sites. Martineau, at the Lourcine, still adhered to the ammoniated peptonate of mercury, of which he gives daily injections, and, as he claims, with excellent results, stating that he had made up to that time two hundred thousand injections in six hundred patients.

Dr. Besnier has since his earlier experiments totally renounced the calomel injections, first on account of the often unavoidable abscesses, and also the stomatitis and enterorrhœa occasionally following them. He thinks that only a minimum of the mercuric chloride formed from the calomel proves efficacious, and that the mercurialization, either by calomel or sublimate, is not more rapid than by other methods, and that relapses are as frequent as they are in the older

ways of administering mercury. Dr. Maurice, as well as Dr. Hallopeau, have frequently noted abscesses after the use of calomel, as well as after the gray oil of Lang, and they confirmed the negative results of Dr. Besnier. Drs. Vidal and Fournier were also opposed to the injections of insoluble mercurials, as recommended by Scarenzio and Smirnoff on similar grounds.

In this country J. C. Wilson has recently treated syphilis and other manifestations according to these methods and with favorable results. It is only quite recently that Professor J. W. Runeberg, of Helsingfors, raises his voice to call attention to the dangers of mercurialization by injections of calomel (*Deutsche Med. Wochenschrift*, January 3, 1889) after Neumann, of Vienna, has pronounced against them as dangerous to health and life.

It is of interest in connection herewith to note the relative value of different mercurials used in the treatment of syphilis. At the Congress für Innere Medizin at Wiesbaden, 1887, Professor Kaposi led the discussion on the therapeutics for syphilis, and to the question propounded, "What are the respective advantages of the different remedies used in the treatment of syphilis?" the following arrangement by Bockhart as to the permanency of curative result was submitted and generally accepted :

1. Most permanent.

- a. Inunctions with unguentum hydrargyri.

- b. Calomel injections.

- c. Lewin's sublimate injections.

2. Moderately permanent.

- a.* Sublimate chloride of sodium injections.
- b.* Albuminate and peptonate of mercury injections.
- c.* Blood serum mercury injections.

3. Less permanent.

- a.* Mercuric cyanide injections.
- b.* Glycocholate of mercury injections.
- c.* Mercury formamidate injections.

After this cursory review of the ups and downs of the hypodermic use of the various mercurials and some of the literature on the subject, I would venture as a deduction from my own experience with the hypodermic use of mercurials in the treatment of syphilis, that in my hands it has certainly produced many striking results. Under my preceptor, Dr. Julius Kaemmerer, I had, together with my friend, Dr. Rosenthal, an opportunity to practise injections of corrosive sublimate according to Lewin's method, perhaps among the first in this country. As early as 1876 and 1877 these injections were made by us daily, and in doses ranging from $\frac{1}{8}$ to $\frac{1}{2}$ grain at a time. In none of these cases, and ever since in many thousand injections of never less than $\frac{1}{8}$ grain, frequently increased to $\frac{1}{3}$ grain, have I been able to find abscesses resulting. In fact, with our present knowledge and ideas of suppuration I can hardly credit the development of pyogenic bacteria possible in a solution of mercuric chloride of the strength of 1 to 100.

Although I have used for some time for the injections a gold needle fitted to an or-

dinary hypodermic syringe encased in hard rubber, a steel needle well anointed will answer as well if properly cleaned and changed as often as corrosion will indicate this necessity. The solution employed by me contains 1 part of corrosive sublimate dissolved in 100 parts of distilled water, of which from twelve to twenty minims are injected daily deep under the skin into the connective tissue, in the region of the back, from above and below the scapula, down to the gluteal region, on both sides and on the sides of the chest. In no case were more than twenty-five to thirty injections made successively, and, as a rule, a total disappearance of the manifestations of early syphilis resulted after the tenth injection. Even late secondary and beginning tertiary cases yielded readily even after other methods of treatment had failed. In all instances the doses were gradually increased until slight gingivitis was experienced, when the amount so injected was diminished until it had disappeared. Enteric or gastric disturbances were only experienced in exceptional cases and when very large doses were exhibited. All of the cases so treated were ambulant and attending to their occupations. Only a small percentage had relapses and had to undergo a second treatment, and only two a third one. An after-treatment with small doses of potassium iodide, 5 grains t. d., or, in place of this, Blanchard's pills of the iodide of iron, followed the injections, and were continued for three months or longer. This is done with a view to inhibit the rapid elimination of mercury following the hypodermic method of soluble mercurials. It is

no longer a doubt that the iodides prevent or retard the elimination of mercury ("Ueber den Einfluss des Quecksilbers auf den Syphilitischen Process," by L. v. Vajda, Vienna, 1880), and the fact that the slower the elimination the greater the safety from relapses is now also generally accepted, and accounts for the permanency of the inunction treatment, after which the presence of mercury in the urine has been detected for a long period, and, in some instances, after thirteen years (Vajda, as above).

The injections of sublimate are painful for a short time afterwards, and leave for some days indurations in the subcutaneous cellular tissue, which occasion inconvenience and distress to the patient. The smaller doses do so in a very moderate degree only. The smallest quantity of sublimate used in a complete treatment by me was 3 grains, while in some of the more serious cases 6 to 8 grains had to be administered to that end.

The patients, as a rule, stand the treatment well, and but few desert on account of it. In order to avoid the pain arising from this method of treatment I have successively experimented with most of the various preparations enumerated above. The albuminate and peptonate of Bamberger I have found quite as painful and not as efficacious as the corrosive sublimate, while the calomel and yellow oxide of mercury injections, though, as by Balzer's directions, suspended in vaseline oil, proved less painful at the time of the injection, and were followed with inflammatory conditions of the connective tissue, which proved most distressing to the patient. The

calomel injections, in my hands, even with the utmost precautions, were often followed by abscesses. The mercuric oxide is in this and its curative effect much preferable, but the pain it gives rise to and the inflammatory indurations are in no respect less, if not more, than with the former. Much might be said and speculated upon the conversion of the mercurials in the tissues, but after all the corrosive sublimate seems to have the most direct bearing upon the pathological cause of syphilis.

When we take into consideration the rapidity with which it causes the symptoms to disappear, when the small amount of mercury introduced into the system is duly considered, and the relative results obtained by it alongside of other, and especially the internal, methods of administering mercurials, it seems surprising that the hypodermic injections of mercurials have taken such slight hold among us.

There is no doubt that the more rapidly the early symptoms of syphilis are brought to abeyance, the greater the immunity from later and more central lesions. I hold, therefore, that next to, and perhaps even before, the unclean and unprecise inunction method, hypodermic injections of corrosive sublimate are by far the best means to reduce the symptoms, and, I believe, cure syphilis in its early stages. That they are painful there can be no question, but if by them and with the endurance of some pain (which is by no means unbearable) we can accomplish in one month what years of ingestion of mercurials often fail to do, and avoid besides the almost cer-

tain impairment of the digestive functions, and prevent later and more central lesions, I think my claim is not overdrawn when I consider the treatment of syphilis by the hypodermic use of mercurials, and especially corrosive sublimate, as the most precise, safe, rapid, and sure of all those heretofore employed.

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